


INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

REC'D 21 OCT 2004

PCT

Applicant's or agent's file reference 418 WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/DK 03/00537	International filing date (day/month/year) 12.08.2003	Priority date (day/month/year) 12.08.2002
International Patent Classification (IPC) or both national classification and IPC C07B57/00		
Applicant H. LUNDBECK AS et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(II) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 04.03.2004	Date of completion of this report 20.10.2004	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Breimaier, W Telephone No. +49 89 2399-8327	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/DK 03/00537**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-77 as published

Claims, Numbers

1-98 as published

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/DK 03/00537**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-98
	No: Claims	
Inventive step (IS)	Yes: Claims	1-68, 84-98
	No: Claims	69-83
Industrial applicability (IA)	Yes: Claims	1-98
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1 : WO 00/12044

D2 : EP-A 0 347 066

The present invention refers to a method for making (es)citalopram via optically active intermediates of general formulae (II) and (IV) which are made available by selective enzymatic acylation and deacylation of the racemates according to claims 1 to 98.

novelty

The subject-matter according to claims 1 to 98 is novel pursuant to art. 33(2) PCT.

None of the documents of the available prior art describes the present method for making (es)citalopram via the optically active intermediates of formulae (II) and (IV) which are made available by selective enzymatic (de)acylation of the racemates according to claims 1-68 and 84-98 as well as the novel intermediates of formula (IV) according to claims 69-83. Novelty is therefore given.

inventive step

The subject-matter according to claims 69 to 83 is considered not to be based on an inventive step pursuant to art. 33(3) PCT.

Intermediates must themselves be based on an inventive step. Whether or not this condition is fulfilled has to be decided by taking the following into consideration. The R- and S- enantiomers of general formula (IV) according to independent claim 69 are novel intermediates for making (es)citalopram which is a well known anti-depressant drug. These intermediates however are considered not to be based on an inventive step in view of the present intermediate state of the art. The R- and S- enantiomers of general formula (II) which are known intermediates for making (es)citalopram (see eg D1, page 6 and D2, page 4) are regarded as equivalents to the claimed acylated derivatives of general formula (IV) which can analogously be used to be cyclised to the above known product.

The present intermediates (IV) are thus thought to be derivable from the prior art in an obvious manner and can not be regarded as being inventive.

The subject-matter according to claim 69 as well as of dependent claims 70 to 83 is considered not to be inventive (art. 33(3) PCT).

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/DK 03/00537

further remarks:

- a. Contrary to clarity (art. 6 PCT), claims 84 to 91 are not dependent on independent process claim 1.
- b. Contrary to Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1 is not mentioned in the description, nor is this document identified therein.
- c. clerical corrections: in claim 10, first line the term "wherein and" is not deleted; in claim 19, line 20 the abbreviation "pfp" is not defined by its proper name (see page 47); in claim 23, line 5, one "wherein" is not deleted; in claim 25, line 13, it does not read "suitably"; in claim 26, line 16 the term "is" is not deleted; in claim 30, second line, it does not read "ethyl or" and in claims 85 and 89 it does not read "derivative".